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PROCEEDINGS  
OF THE  
PATHOLOGICAL SOCIETY  
OF  
PHILADELPHIA

New Series, Vol. XI.

February, 1908

No. 2

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PUBLISHED BY THE SOCIETY

384 South Sixteenth Street

1908



# Proceedings of the Pathological Society of Philadelphia.

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### **Significance of Tubercle Bacilli in the Feces.**

By RANDLE C. ROSENBERGER, M.D.

(From the Clinical Laboratory of the Philadelphia Hospital.)

THE detection of tubercle bacilli in solid or well-formed stools of several patients, whose histories were vague and in whom the clinical diagnosis was far from clear, led the writer to take up this subject for research.

The idea was to actually see how prevalent the occurrence of acid-fast bacilli in the feces was by studying the feces of others than those suffering from known tuberculous infection. With this end in view, during the past two years 612 cases were collected from the wards of the Philadelphia Hospital. Together with this number there were stools of 60 cases of diagnosticated tuberculous infection, making in all 672. The stools were obtained from patients with croupous pneumonia, typhoid fever, erysipelas, diarrhea, surgical and nervous cases, and from individuals who were apparently healthy; in fact, from patients in all wards of the institution, no matter what the clinical diagnosis. Of these stools, 137 were solid, 297 were semisolid, and 178 were fluid. The tubercle bacillus was found in 120 cases, or 19.6 per cent.; in solid stools 28 times, in semisolid stools 40 times, and

in fluid stools 52 times. In the 60 cases of diagnosticated tuberculosis the organism was demonstrable in all, no matter what the consistency of the feces.

It has been observed by some that acid-fast bacilli have been found in the feces of those suffering from enteric fever, and that it is quite common for them to be found in all specimens of feces, even in health; that this latter assertion is absolutely erroneous will be shown by the results of the studies here recorded. The presence of the tubercle bacillus in the feces may be a process of excretion, so a few experimental studies regarding the excretion of bacteria in general may be quoted.

Newmann (*Berl. klin. Woch.*, 1890, p. 229) and Karlinski (*Prager med. Woch.*, 1890, p. 231) observed the *Bacillus typhosus* in the urine in 35 out of 112 cases examined. Wyssokowitsch (*Zeits. f. Hyg.*, 1886, vol. i, p. 3, quoted by Sherrington), in 22 experiments, employed; 14 bacterial species, only twice were the species introduced into the blood, and yet they were found in the contents of the intestine. On each occasion there were macroscopic hemorrhages in the serosa and mucosa. He concludes that the passage of bacteria into the excreta occurs only when the blood containing them escapes through some breach of continuity in the excretory membrane due to inflammatory or mechanical injury. Dobroklouski (quoted by Sherrington, *Jour. Path. and Bact.*, 1893, p. 258), in Cornil's laboratory, found that the bacillus of avian tuberculosis, when administered with food, infected guinea-pigs by penetrating the healthy intestinal mucosa.

As corroborative evidence, numerous investigators have performed experiments by feeding, by subcutaneous and intravenous inoculations, and proved that the organisms reach and pierce the mucous membrane without any evident lesion being present.

Emmerich and Buchner (*Arch. of Hyg.*, vol. ii, p. 357), after injecting the *B. neapolitanus* into the blood, found that the organism escaped in large numbers through the intestinal wall. In one experiment no pathological change in the intestinal wall was observable, but in almost all there was blood in the contents of the intestine and hemorrhages in the mucosa. Sherrington (*Jour. Path. and Bact.*, 1893, p. 276), in concluding his article on the escape of bacteria with

the secretions, says the evidence is against believing that when the transit of bacteria across the secreting membrane occurs the membrane is still normal in condition, although at the same time it may not be ruptured or pervious to red blood cells.

The fact that the escape of the bacteria tends to occur not immediately upon the introduction of them wholesale into the circulation, but in the late stages of the communicated disease, suggests that the healthy secreting membranes are not pervious to bacteria, and that only after soluble poisons produced by the infection have had time to act upon them do the membranes become pervious to the germs.

Babes (*Comp. Rend.*, Paris, 1888) concludes from experimental work upon glanders that the bacillus can penetrate uninjured mucous membranes. At this point may be mentioned the well-known experiments of Ravenel, who, shortly after having fed animals tubercle bacilli, killed them and found the bacilli in the thoracic duct, though no lesions or abrasions of the mucous membrane of the gut were evident.

As another instance of the penetration of mucous membranes by pathogenic organisms, typhoid bacilluria may be mentioned. This condition was studied at some length by Koujojeff (*Central. f. Bact. u. Parasit.*, 1889, vol. vi, p. 672), by Charrin and Ruffer, Ruffer, Schweiger, Blachstein, Corrado, Pernice and Scagliosi, Cornil, and others quoted by Sherrington (*loc. cit.*). They have proved by experiments upon animals with various bacteria that it is quite common for bacteria to be found in the bile or urine after intravenous or subcutaneous inoculation, or even through feeding.

I inoculated rabbits and guinea-pigs subcutaneously with a homogenized culture of attenuated tubercle bacilli. Upon the fourth day I detected tubercle bacilli in their feces. After seven weeks the animals were killed. The guinea-pig showed neither a local nor visceral lesion, not even intestinal lesions, while the rabbit, though no visceral lesions were found, had a caseous mass at the site of inoculation and in the right inguinal region. A second series of guinea-pigs and rabbits were inoculated in the same manner and with the same organism. I again found tubercle bacilli in their feces at the end of the fourth day. These animals were killed at the end of the

sixth week, and at autopsy no intestinal, visceral, or glandular lesions were present in the guinea-pig, but the rabbit showed a large, apparently caseous mass in the right inguinal region, in which I was unable to find tubercle bacilli.

Examination of a number of specimens of feces from guinea-pigs and rabbits in apparent health failed to reveal any acid-fast bacilli.

In well-defined instances of pulmonary tuberculosis it is the rule to find tubercle bacilli in the feces. If a case comes under the observation of the clinician which is not at all clear, presenting a clinical picture resembling malaria, enteric fever, or acute miliary tuberculosis, the finding of tubercle bacilli in their feces will determine the diagnosis.

In those suffering from chronic diarrhea, with no other appreciable symptoms, pulmonary or otherwise, the tubercle bacillus is at fault in most cases. These cases have frequently come to autopsy, some showing intestinal ulceration and others showing no ulceration.

Instances of ascites, the exact nature of which was unknown, were diagnosticated positively as tuberculous by the finding of the tubercle bacillus in the feces. These cases were further proved by surgical procedures, *i. e.*, abdominal operation. As a well-marked intestinal tuberculous ulcer is appreciable from the appearance of the serous coat of the gut, in one case thus operated upon no ulcers were present.

That the tubercle bacilli are in the feces, irrespective of a pulmonary or an intestinal lesion, is proved by the fact that I found them in cases of general glandular involvement, meningitis, hip-joint disease, and in Pott's disease of the spine, the latter condition being in a boy, aged five years. In acute miliary tuberculosis, diagnosticated or not diagnosticated, clinically, the bacillus was present in the feces in all cases. The result of these studies suggests the intestinal mode of infection in tuberculosis in general. It is my intention merely to quote a few observations supporting the theory of the intestinal infection in tuberculosis, as these studies strengthen that theory. This theory of infection is gaining ground daily, and the experiments of Schroeder and Cotton (*Bull. No. 86, Bureau of Animal Industry of Dept. of Agriculture*), of Ravenel and of Vallee, who practically confirmed Ravenel's feeding experiments by working upon calves;

of von Behring, of Calmette and Guerin's work upon goats, demonstrate fully that the intestine is by far the most common path of infection, and that aërial infection is uncommon.

In a number of autopsies, in which the mesenteric and other glands were studied bacteriologically, it was found that over 40 per cent. showing no tuberculous lesions in any part of the body were tuberculously infective. It was also found that in all cases of active tuberculosis, and in almost all cases of inactive tuberculosis, the mesenteric glands were tuberculously infective (Rosenberger, "A Study of the Mesenteric Glands in Their Relations to Tuberculosis," *Amer. Jour. Med. Sci.*, July, 1905). Supporting von Behring's theory that the most frequent method is through the intestinal wall, Guthrie found over 22 per cent. of infections through the intestinal tract, Heller nearly 40 per cent. of primary intestinal affections, and Still over 23 per cent.

To explain the presence of the tubercle bacillus in the feces of man is not easy.

The writer believes that the bacillus enters the human economy through ingestion, water (?), either in infancy or maturity. At first the number of bacilli is not large, and they find their way to the blood and lymph stream. During their transit some are discharged through the feces and others through the urine.

The circulation of these organisms through the lymph and blood continues indefinitely, and the patient actually suffers from a toxemia which may be so severe as to set up chronic diarrhea, or cause vague symptoms characteristic of no one disease.

As the organisms multiply in the body, and as the toxemia and irritation progress, a point of least resistance is somewhere established, the tubercle bacillus lodges and sets up the disease with its distinct pathological features. It is interesting to note that in cases of healing tuberculosis, or actually arrested or healed cases, the tubercle bacillus is rarely if ever found in the feces. This is also true of the occurrence of tubercle bacilli in the sputum. In some of these cases recorded, the sputum has been examined at least six and as many as twelve times negatively and subsequent examination of the feces was also negative.

Passler (*Münch. med. Woch.*, October 23, 1906), in considering

the diagnosis of pyretic conditions, as septicemia and typhoid, mentions the probability of acute intestinal tuberculosis as the cause of the malady, irrespective of tuberculosis of any other organ. During the evolution of intestinal tuberculosis, he suggests that the infection by pyogenic organisms will perform the same role as they do in ulcerative pulmonary tuberculosis, and asserts that when we are dealing with a marked pyretic condition, which has lasted for several weeks without any particular and definite signs to indicate typhoid fever or septicemia, we must always think of an acute intestinal tuberculosis. He concludes by saying that as an intestinal infection may occur without any manifestations clinically, the feces should be examined for the presence of tubercle bacilli. (He cites only two cases.)

Wood (*Chemical and Microscopic Diagnosis*, 1905) states that tubercle bacilli are found in the feces of persons suffering from tuberculosis (pulmonary), because in the majority of cases the bacilli are swallowed, together with small masses of sputum.

Sahli (*Diagnostic Methods*, 1905) mentions that in intestinal tuberculosis tubercle bacilli are found in the feces, and are therefore of diagnostic importance. The stools may, however, contain these bacilli even though there is no intestinal tuberculosis (if the patients swallow their sputum). Searching the stools has even been recommended for the diagnosis of lung tuberculosis in cases of irresponsible persons who swallow the sputum. Previous treatment with dilute potassium hydroxide or digestive enzymes is often successful and may be serviceable in the examination of mucopurulent particles of the movement which have been isolated from the mass of feces. We do not know whether under certain conditions decomposition will destroy tubercle bacilli in the intestine. At any rate, we cannot always demonstrate tubercle bacilli in the stools, even when there is undoubted intestinal tuberculosis. Perhaps this is on account of the dilution of the content of tubercle bacilli by the abundant particles of food. Tubercle bacilli are most readily found in the purulent or bloody pieces of diarrheal stools. As tubercle bacilli in the feces may be due to swallowed sputum, we can diagnosticate intestinal tuberculosis if bacilli are found in the feces only when at the same time attacks of diarrhea occur with pus and blood in the

stool. The tubercle bacillus must be carefully distinguished from the smegma bacillus, which is said to occur at the anal orifice and might have become mixed with the feces.

Lichtheim (*Fortschritte Med.*, January, 1883) says that the presence of tubercle bacilli in the stools is the exception rather than the rule in persons suffering from pulmonary tuberculosis. He further asks the question whether the presence of these organisms in the feces means intestinal ulceration or merely that the patient has swallowed them with his sputum. In control observations he showed this not to be the case, as he claimed it was only exceptional to find the bacilli, as they were very difficult to find, and then only a very few were present.

In January, 1897, Shaw (*Jour. Amer. Med. Assoc.*, March 20, 1897, p. 554) mentioned the finding of tubercle bacilli in the feces of a patient exhibiting no tuberculous lesion of the intestinal tract. The lungs, however, showed isolated tubercles and areas of bronchopneumonia.

Emerson (*Clinical Diagnosis*, 1906, p. 390), in remarking upon the occurrence of tubercle bacilli in the feces, says that it must always be borne in mind that the organisms may be swallowed, and this especially so in children in whom the diagnosis of pulmonary tuberculosis has been made; "but this is rather a remote possibility in the case of a careful adult."

Boston (*Clinical Diagnosis*, 1904, p. 380) recommends collecting a "small portion of the purulent or mucoid material from the feces, smear it thinly on a slide," and then stain for tubercle bacilli, as in the sputum. "Tubercle bacilli when found in the feces point conclusively to the existence of tuberculous ulceration of the intestines."

Simon (*Clin. Diag.*, 5th ed., 1904, p. 328) claims that when tubercle bacilli are present in the feces it indicates intestinal ulceration, providing they are observed upon repeated examinations and there are clinical symptoms pointing to the bowels as the seat of the disease; otherwise, they may be referable to swallowed sputum.

TECHNIQUE.—If the specimen to be examined was a fluid or semi-solid one, a small quantity from any part of the stool was taken and spread on a slide, dried, and stained. When the feces were solid,

a small amount of sterile distilled water was put upon the slide and a small mass of fecal matter mixed thoroughly, spread, dried, and stained. Not one of the specimens was centrifugalized.

In staining the preparation, carbol fuchsin was applied for fifteen minutes in the cold, the excess drained off, and Pappenheim's solution poured on the preparation. This was allowed to act for two or three minutes, washed with water, and if the specimen was of a uniform blue color it was dried and examined in cedar oil. If the preparation was not uniformly blue, Pappenheim's solution was applied and reapplied until the smear was blue. By observing this technique carefully no mistake can happen regarding the diagnosis of the tubercle bacillus, as this organism and spores of other bacilli are the only bodies retaining the carbol fuchsin stain. All other bacteria and cellular elements are stained blue. Great care must be taken lest some artefact be mistaken for the tubercle bacillus, such as a minute scratch in the glass, a small crystal, or the periphery of a cell. The organisms, as a rule, are comparatively few in cases not plainly diagnosed as tuberculous, but in well-marked cases of pulmonary or intestinal tuberculosis they are comparatively abundant. The finding of the tubercle bacillus in a spread is not always easy of accomplishment; it has frequently taken the writer at least an hour, and sometimes as long as two hours, to find three or four bacilli.

Direct searching through solid stools is less promising than in fluid stools. Nevertheless, tubercle bacilli may quite frequently be demonstrated in solid movements if, as Hamburger (quoted by Sahli) recommends, we mix a piece of feces the size of a pea with a few centimeters of water, then centrifuge gently to remove the coarser pieces, dilute the supernatant cloudy fluid with a double volume of alcohol, centrifuge once more, and then after drying examine the remaining precipitate, which will consist almost exclusively of bacteria. (Personally, I have never found this procedure necessary.)

Park (*Pathogenic Microorganisms*, 1905, p. 312) recommends searching in the feces for any purulent or mucous particles, and if none are found the larger masses are removed, the rest diluted and centrifugalized, and stained by the ordinary methods.

Page (quoted by Emerson) mixes a small mass of feces in 1.5 c.c.

distilled water, adds 54 c.c. of a mixture of equal parts of alcohol and ether, centrifugalizes ten minutes, makes a smear of the sediment, fixes it to the slide with albumin, and stains as usual.

If the assertion that tubercle bacilli found in the feces result from swallowing sputum, or the presence of intestinal tuberculosis is true, the examination of the feces is useless, as no further knowledge is gained.

It is a well-known fact to students of tuberculosis that a persistent diarrhea is present for a very long time, and yet the autopsy shows no ulcerations in any part of the intestinal canal. Therefore, it is by no means pathognomonic that, if we find tubercle bacilli in the feces of those suffering from tuberculous enteritis, ulcerative lesions are present. But suppose that acid-fast bacilli are present in the feces of a person not suffering from any appreciable lesion of tuberculosis. What then is the significance of such a finding?

To the writer it has been proved from the studies made of this number of cases, both from a clinical and pathological standpoint, that if an acid-fast bacillus is present in the feces of any individual, and this organism resembles morphologically and tinctorially the tubercle bacillus, tuberculosis of some part of the body exists.

I do not mean pulmonary tuberculosis, but tuberculosis of the intestines, liver, lymph nodes, peritoneum, or any viscus. A *resume* of some of the cases that came to autopsy, with general remarks of those who did not succumb to the disease, is of great interest and very instructive.

In almost two-thirds of the cases I was fortunate in being able to follow up the clinical findings with those at autopsy. A small percentage of cases were removed from the institution in a precarious condition, and although a number of cases died, no autopsy was permitted.

I wish to extend my thanks to the various resident pathologists at the Philadelphia Hospital for their valuable coöperation in the work.

CONCLUSIONS.—1. No other acid-fast bacillus was found in the feces but the tubercle bacillus.

2. The presence of the tubercle bacillus in the feces means that active tuberculosis exists somewhere in the economy.

3. In acute miliary tuberculosis the bacillus is always present in the feces.

4. In all cases of chronic diarrhea and in cases of general glandular involvement the feces should be examined for tubercle bacilli.

5. The finding of tubercle bacilli in the feces does not mean intestinal ulceration in all cases.

6. In arrested or healed pulmonary tuberculosis no tubercle bacilli are found in the sputum or feces.

7. The feces should be studied for tubercle bacilli as a part of the routine examination, especially in suggestive cases and where no expectoration can be obtained.

*Resume* of cases in which tubercle bacilli were found in the feces irrespective of the clinical diagnosis, with findings at autopsy, and with general remarks on those that did not come to the autopsy table:

1. Clinical diagnosis, cirrhosis of liver with ascites. There was no expectoration. Three days before death delirium set in, suggesting meningitis. At autopsy, miliary tuberculosis of lungs and tuberculosis of the peritoneum; no intestinal ulcerations.

2. Clinical diagnosis, chronic pleurisy. Eleven examinations of sputum were negative. At autopsy pleura was one-eighth of an inch in thickness over right lung, and the same lung showed miliary tuberculosis; no intestinal ulcerations.

3. Clinical diagnosis, acute miliary tuberculosis. Sputum examined on nine occasions with negative results. At autopsy miliary tuberculosis of lungs and spleen; no intestinal ulcerations.

4. Clinical diagnosis, acute miliary tuberculosis. At least six examinations of the sputum were negative for the tubercle bacillus. At autopsy there was found acute miliary tuberculosis of all the viscera; no intestinal ulcerations.

5. Clinical diagnosis, pleurisy and tuberculosis of hip. Sputum on a number of occasions was negative for the tubercle bacillus. At autopsy there was acute miliary tuberculosis of all viscera; no intestinal ulcerations. (Three weeks after finding the tubercle bacillus in the feces it was found in the sputum.)

6. Clinical diagnosis, typhoid fever. No expectoration, and there were four negative Widal reactions. At autopsy, six small irregular atypical ulcers, long axis transverse to bowel; one of these ulcers

had perforated the gut. Studied bacteriologically, these ulcers showed few tubercle bacilli.

7. Clinical diagnosis, tuberculosis of the hip. No autopsy.

8. Clinical diagnosis, acute miliary tuberculosis. Acute miliary tuberculosis of all viscera found at autopsy but no intestinal ulcerations.

9. Clinical diagnosis, croupous pneumonia and pleurisy. No tubercle bacilli found in the sputum. Crisis occurred, but the patient is still running an irregular temperature.

10. Clinical diagnosis, chronic diarrhea. No cough, no expectoration. No autopsy.

11. Clinical diagnosis, chronic diarrhea. After finding tubercle bacilli in the feces, slight impairment of resonance was noted in the right apical region.

12. Clinical diagnosis, chronic diarrhea and cirrhosis of the liver. No expectoration. Tuberculous ulcers were found in the gut at autopsy.

13. Clinical diagnosis, repeated attacks of pleurisy. No expectoration. No autopsy.

14. Clinical diagnosis, pleurisy with effusion. Sputum negative on four occasions for the tubercle bacillus.

15. Clinical diagnosis, chronic diarrhea. No expectoration. Typical tuberculous ulcers of the gut were found at autopsy.

16. Clinical diagnosis, erysipelas and diarrhea. No expectoration. Slight pulmonary lesions were found; no intestinal ulcers.

17. Clinical diagnosis, septicemia? pelvic abscess? typhoid? Acute miliary tuberculosis of all viscera; no intestinal ulcers.

18. Clinical diagnosis, malignant endocarditis. No expectoration. Acute miliary tuberculosis of all viscera; no intestinal ulcers.

19. Clinical diagnosis, chronic diarrhea. At autopsy, intestinal ulcers were found.

20. Clinical diagnosis, alcoholism. No expectoration. Recent and old lesions were present in the lungs; no intestinal ulcers.

21. Clinical diagnosis, tuberculous peritonitis. At autopsy, tuberculous peritonitis and intestinal ulcers were found.

22. Clinical diagnosis, pleurisy. Tuberculosis of both pleuræ,

of mesenteric glands and spleen; no pulmonary or intestinal lesions found.

23. Clinical diagnosis, chronic diarrhea. Tuberculous ulcers present.

24. No clinical diagnosis made. At autopsy general miliary tuberculosis was found, but no intestinal lesions.

25. Clinical diagnosis, enteritis. This case was a child, aged two years, treated for seven months for gastro-enteritis; there was no cough, no expectoration; the cervical glands were enlarged.

26. Clinical diagnosis, tuberculous peritonitis. Patient had cavities in both lungs, yet no sputum could be collected.

27. Clinical diagnosis, Pott's disease. This case was a child, aged five years; no pulmonary lesions demonstrable. No autopsy.

28. Clinical diagnosis, typhoid fever and pneumonia. No tubercle bacilli were demonstrable in the sputum on several different occasions, and during illness two negative Widal tests resulted, and blood showed a leukocytosis of 17,000. At autopsy, acute miliary tuberculosis of both lungs, liver, and spleen, with few intestinal ulcers.

29. Clinical diagnosis not made. At autopsy, general miliary tuberculosis; no intestinal ulcers.

30. Clinical diagnosis, tuberculous peritonitis. This case was operated upon and the diagnosis confirmed.

31. Clinical diagnosis, probable carcinoma of the stomach. Pernicious vomiting, chronic diarrhea, marked cachexia, and emaciation were among the cardinal symptoms. No autopsy.

32. Clinical diagnosis, typhoid fever. Child, aged six years, running a persistent irregular temperature, no pulmonary symptoms, and three Widal tests were negative.

33. Clinical diagnosis, secondary anemia. Besides the tubercle bacillus being found in the feces, the ova of the tricocephalus dispar and ascaris lumbricoides were present. The malarial parasite was also seen in the blood. (As this was an immigration case, he was immediately deported.)

34. Clinical diagnosis, probable tuberculosis of the liver. Bacilli were found on two occasions in the feces. No autopsy.

35. Clinical diagnosis not made. Sputum examination negative

on three occasions. Caseous tuberculosis of the bronchial and mediastinal glands; miliary tuberculosis of the kidney, liver, spleen, and intestines was found at autopsy.

36. Clinical diagnosis, chronic pleurisy. No tubercle bacilli were found, in the sputum. At autopsy adhesive pleurisy on both sides was found, together with a few miliary tubercles in the lung. There was no intestinal ulceration.

37. Clinical diagnosis, erysipelas. No tubercle bacilli were demonstrable in the first three examinations of the sputum, though a fourth examination was positive. (Three days after tubercle bacilli were found in the sputum pulmonary hemorrhage took place and the bacillus was found at this time.)

38. Clinical diagnosis, interrupted recovery from typhoid fever. No autopsy.

39. Clinical diagnosis, typhoid fever. Acute miliary tuberculosis of general character was found at autopsy; no intestinal ulcerations.

40. Clinical diagnosis, chronic diarrhea. Tuberculosis of the intestines and tuberculosis of the mesenteric glands was present at autopsy.

41. Clinical diagnosis, acute miliary tuberculosis. No tubercle bacilli were found in the sputum. At autopsy acute miliary tuberculosis of all the viscera was found, but no intestinal ulcers.

42. Clinical diagnosis, chronic diarrhea and jaundice. X-rays showed gallstones. Tuberculosis of the retroperitoneal glands was observed at autopsy, but no gallstone.

43. Clinical diagnosis, pneumonia. No crisis, and running an irregular temperature. No tubercle bacilli could be found in the sputum. Healed tuberculosis of the lungs, with tuberculous ulcers in the gut, was found at autopsy.

44. Clinical diagnosis, typhoid fever. No expectoration. At autopsy acute miliary tuberculosis of a general character was found.

45. Clinical diagnosis, carcinoma of the liver. At autopsy cancer of the lung and liver was found, together with tuberculosis of the mesenteric glands.

46. Clinical diagnosis, locomotor ataxia, with empyema. One liter of pus was found in the pleural cavity at autopsy. There was

one positive and two negative examinations of the sputum for tubercle bacilli.

47. Clinical diagnosis, general glandular enlargement. Spreads from an inguinal gland removed during life showed tubercle bacilli, and spreads from a mesenteric gland removed at autopsy also contained tubercle bacilli. At autopsy there was no pulmonary tuberculosis, but a purulent peritonitis, with general enlargement of all lymphatic structures. No intestinal ulcers.

48. Clinical diagnosis, typhoid fever. At autopsy, tuberculous ulcers were observed; no pulmonary lesions.

49. Clinical diagnosis, tuberculous peritonitis. Operation disclosed fibrinopurulent peritonitis. Numerous miliary tubercles on visceral and parietal layers of the peritoneum were observed, but no intestinal ulcerations could be made out.

50. Clinical diagnosis, malaria. Patient has had chills, fever, and sweats occurring almost daily for ten days. Examination of the blood on several occasions failed to demonstrate the malarial parasite.

51. Clinical diagnosis, meningitis. Child, aged eighteen months. No pulmonary symptoms. Tubercle bacilli were demonstrable in the spinal fluid about the same time they were found in the feces.

52. Clinical diagnosis, cervical lymphadenitis. Upon the second examination, and after a very careful and prolonged search, a few tubercle bacilli were found in the feces.

53. Clinical diagnosis, cutaneous tuberculosis (lupus). Although tubercle bacilli were found in the feces, no pulmonary lesions could be made out.

54. Clinical diagnosis, diarrhea alternating with constipation. No autopsy.

55. Clinical diagnosis, gunshot wound of the chest penetrating the lung. On five occasions the sputum was examined for tubercle bacilli, but with negative results. At autopsy a large cavity was found which was surrounded by gangrenous tissue, and on the margin, upon histological examination, tubercles were found which showed few tubercle bacilli.

56. Clinical diagnosis, tumor of testicle, probably tuberculous. The organ was removed, and histologically presented a typical picture

of tuberculosis. No pulmonary lesions were evident. It might also be mentioned that tubercle bacilli were found in sections of the organ and also in spreads before fixation.

57. This case was one in which a large ulcerating mass was present in each groin, involving the inguinal glands. The condition had persisted for two years. Tubercle bacilli were found in the feces, though the condition had been diagnosticated as sarcomatous, specific, and tuberculous. Sections of the masses studied histologically showed typical tubercles and giant cells and tubercle bacilli.

Besides these cases just cited there were nine cases of chronic diarrhea, certain of which, upon autopsy, showed tuberculous ulcers and others did not. In a few of these latter cases slight pulmonary involvement could be seen, while in the greater number no pulmonary lesions could be made out.

#### DISCUSSION.

DR. W. T. LONGCOPE wished to know whether the bile of tuberculous patients had been examined for tubercle bacilli. This question was suggested to him by the fact that typhoid bacilli were so frequently found in bile.

DR. DAVID RIESMAN asked whether the feces of patients with lupus had been examined for tubercle bacilli.

DR. W. W. HAWKE referred to a case in the Insane Department of the Philadelphia Hospital. A man who had been gaining in weight for the past two years had developed what was thought to be a rectal irritation from seat worms. Physical examination revealed a friction in the upper right quadrant of the abdomen which was thought to be produced by the colon slipping over the surface of the liver. Two specimens of the feces were examined and tubercle bacilli found in both. There were no definite outspoken signs of tuberculosis, though a suspicion of an attenuated form of tuberculosis was being entertained.

DR. JOSEPH MCFARLAND asked whether other tests than the morphology and staining characteristics had been used to prove that the organisms found were tubercle bacilli. He thought it incon-

ceivable that tuberculous lesions so obscure that definite signs were not present should discharge bacilli into the intestinal tract in such numbers as to be found as reported.

DR. H. R. M. LANDIS, referring to similar examinations on the feces of tuberculous patients at the Phipps Institute, stated that it was his opinion that practically all patients with pulmonary tuberculosis swallow some tubercle bacilli. These could be detected in the feces, showing that tuberculous ulcerations in the intestine were not necessary to have the bacilli in the stools.

DR. ROSENBERGER, in answer to questions and in closing, stated that seventeen specimens of bile from tuberculous patients had been examined, with negative results. He had only been able to secure one case of lupus without pulmonary lesions, and this one had shown tubercle bacilli in the feces. No other test than the morphology and tinctorial characteristics of the organism had been applied to the bacilli found. Several attempts had been made with animal inoculation, but all had failed, owing to the death of the animal from septicemia. The organism most apt to be confused with the tubercle bacillus would be the smegma bacillus, and this could be differentiated by the method used. Pappenheim's solution after staining with carbol-fuchsin will decolorize this organism in twenty minutes.

### **Squamous-celled Carcinomata of the Esophagus.**

By W. TAYLOR CUMMINS, M.D.

(From the Pathological Laboratory of the University of Pennsylvania.)

WITH regard to the type of cell, carcinomata of the esophagus are divided into two classes, the squamous-celled and the columnar-celled. The former are much more frequently found, for, in fact, cases of the latter type are rarely encountered. For the most part the tumor is primary in this organ, but cases are reported in which it is the seat of metastatic deposits from the pharynx, thyroid, and cardia of the stomach. The esophagus appears to be invaded but rarely by cancerous growth, for out of a series of 722 cancers<sup>1</sup> in all parts of the body

only 6 were found in the esophagus. It seems to enjoy a certain degree of immunity from neoplastic invasion in contrast with the organs lower in the alimentary tract. Zenker and von Ziemssen<sup>2</sup> have collected reports of 5079 autopsies, of which 0.36 per cent. showed esophageal cancer, and of these 0.25 per cent. were primary.

The organ may be divided very conveniently into three segments, viz., an upper or cervical, a middle or thoracic, and a lower or diaphragmatic portion. Bland-Sutton<sup>3</sup> believes that the location of the neoplasm may determine whether it is of the squamous-celled or columnar-celled type, the former electing the upper two-thirds and the latter the lower third of the tube. This statement must not be made dogmatically, owing to the fact that statistics reveal many instances in which the squamous-celled tumor primarily involved the lower third of the organ. As to the point of greatest frequency of involvement there seem to be widespread differences of opinion. It is conceded that the points of narrowing of the tube are the usual seats of the new-growth. These are found at the levels of the cricoid cartilage, the bifurcation of the trachea and of the diaphragm. Possibly localized trauma at these apparently stenotic areas may incite tumor formation. Upon making a *resume* of the statistics at hand there is revealed the fact that the new-growths, including both types, are somewhat more frequently found in the lower third of the organ. Kraus<sup>4</sup> collected 901 cases, and of these 397 were found in the lower third, 302 in the middle, 158 in the upper third, and 45 involved more than one part of the organ.

The esophageal tumor may be small and definitely circumscribed, or, on the other hand, it may be quite large, with imperfect demarcation. In some instances multiple foci have been observed. There is usually some stenosis of the tube, but in a few reported cases this condition was absent. Ulceration and cicatrization are likely to develop and in many cases the lumen of the gullet is almost obliterated. In those cases in which the carcinoma involved the diaphragmatic segment, Bland-Sutton has explained the forcible ejection of food after swallowing by the fact that the tube assumes a spindle shape on account of the stenotic condition and there occurs an hypertrophy of the muscular walls immediately above, thus favoring a forcible regurgitation of the esophageal contents.

The squamous-celled cancer is found much more frequently in men than in women. Bland-Sutton has observed it four times more frequently, while Mackenzie, Zenker, and von Ziemssen have found it three times more frequently in men. The distribution in the sexes appears comparable to that of neoplasms of the stomach. Age seems to be a factor in its production. The prolific period is between forty and sixty years, while cases are recorded as early as the thirtieth year, and as late as the eighty-fourth year. A few exceptional cases are on record in which the disease appeared in the nineteenth and twenty-first years. Curiously, the female sex seems to be attacked earlier in life than the male.

It has been said that carcinomata of the esophagus do not often metastasize. This has been explained by the fact that the disease is often rapidly fatal and metastases have not had the opportunity to develop. Certain it is that the patient, in many instances, is not long under observation subsequent to the development of localized symptoms, and death may take place from inanition, exhaustion, or septic pneumonia. Reports of metastatic growths are noted rather infrequently. The posterior mediastinal glands appear to be affected more frequently than any of the other structures, and their position renders easy access of tumor tissue from the thoracic segment of the gullet. Of 55 cases<sup>5</sup> of esophageal carcinomata recorded at St. George's Hospital, London, these glands showed metastatic deposits in 24 cases. Evidences of metastases were observed in the liver in 10 cases, in the lungs in 6 cases, in the kidneys in 5 cases, in the bones in 4 cases, and in the adrenals and spleen in 2 cases each. Widespread dissemination of the cancerous elements is distinctly rare. In a few cases reported in literature the tumor had existed for years without producing secondary foci, and they were generally of the flat-celled type.

Among those who have reported upon cancer of the esophagus with metastases are Burnet,<sup>6</sup> Butlin,<sup>7</sup> Wright,<sup>8</sup> Scott,<sup>9</sup> and Eskridge.<sup>10</sup> Cancer statistics have been collected by Gillies<sup>11</sup> and Moak.<sup>12</sup>

PERSONAL OBSERVATIONS. These have been confined to a review of the autopsy records on file at the Pathological Laboratory of the University of Pennsylvania from 1874 to 1907. The number of records examined was 1993, and of these 10 showed squamous-celled carcinomata of the esophagus, distributed as follows: 1 in 1891, 1 in 1893,

4 in 1901, 1 in 1904, 2 in 1906, and 1 in 1907. In regard to the prevailing sex, the males outnumber the females, 8 to 2. This conforms with the assertions made by the other investigators that these neoplasms are much more frequent in men than in women. The ages ranged from thirty-four to seventy-four years. The youngest cases aged thirty-four and thirty-eight years were females, while the youngest male was fifty. It appears that the disease may develop earlier in life in the female than in the male. In but 6 of the 10 cases was the race noted, and all of them were white. Nothing conclusive appears in literature with regard to the comparative frequency of the condition in the races. As to the points of predilection in the esophagus, as already stated, there appear to be differences of opinion. In 7 cases only was the site of the primary tumor indicated, and 4 of these involved the lower third of the tube. Some of the statistics are based upon all cancers of the esophagus, while personal observations were made upon the squamous-celled type alone. The results are comparable from the fact that the indifferent type, the columnar-celled, is so infrequently encountered. All of the tumors of this series appeared to be primary in the esophagus, and involvement of not more than one segment had occurred. As to the general character of the tumors, 4 showed considerable ulceration, 3 were fungoid, and 1 was characterized by dense cicatrization of the esophageal walls. In 2 cases the appearance of the tumor was not noted on the records.

The number of cases presenting metastases outnumbered those without 6 to 4. This surely does not show a comparative rarity of metastases in such tumors. For the most part, the notes upon the gross anatomy of the organs were disregarded, and the diagnosis was determined by the histological findings. Metastatic growths occurred in the organs with the following frequency: Stomach, four times; liver, three times; pancreas, three times; lungs, twice; posterior mediastinal glands, twice; bronchial glands, twice; hepatic glands, twice; kidneys, once; pancreatocapsular and lumbar glands, each once. The most widespread metastases occurred in Case II, in which foci were found in the liver, lungs, stomach, pancreas, hepatic, pancreatocapsular, and bronchial glands. Histologically the primary and secondary growths were divided into two groups dependent upon the presence or absence of "epithelial pearls." In view of the fact that

the keratinous structure of the squamous epithelium of the esophagus is poorly developed, the presumption might be that tumors involving such a tissue would usually show an absence of "pearls." Such was not the case in this series, for 5 showed the presence and 3 the absence of "pearls." In 2 cases this point was not noted in the records.

It seems plausible that the facts pertaining to the development of the tumors of the spinal and basal cellular types of carcinomata of the skin might readily apply to these tumors, *i. e.*, the tumors in which the superficial strata of epithelium are directly concerned show "epithelial pearls," while those in which the epithelium of the deeper or basal strata has proliferated show no "pearls." In the secondary as well as in the primary growths the nests of tumor cells were much smaller in those cases showing "epithelial pearls" than in those in which they were absent. In several of the metastatic deposits in the latter group the squamous character of the cells was made out with some difficulty. Those cases which showed "pearls" in the esophageal tumor showed the same in the secondary tumors. However, there appeared a tendency toward a diminution in size, and this was well shown in the tumor of the kidney (Case VII), in which the "pearls" could with difficulty be recognized. It was thought by the author that a comparison of the frequency of metastases in those primary tumors with and without "pearls" might reveal less frequent metastases in those with "epithelial pearls." Examination of the records reveals that of the 4 cases without metastases 3 showed "pearls." So limited a number of cases makes it problematical, but at least suggestive.

Several of the tumor sections presented rather unusual features. In one, a section of lung, there was shown embolism of the smaller radicles of the pulmonary arteries by masses of squamous epithelium. The deposits were confined to these locations, and but few of them were seen. In a pancreas there was infiltration of a small lobule by squamous epithelium, with the Island of Langerhans vaguely evident. In a kidney the cortex showed a large, irregularly rounded mass composed of small nests of squamous epithelium with very small, deeply stained "pearls."

**METASTASIS.** Under this heading a brief description of the lymphatic system of the esophagus and neighboring structures is indispensable. The lymphatics of the esophagus fall into two groups—viz.,

those in the submucosa and those in the muscular coats. The cervical portion of the organ drains into the superior deep cervical and recurrent nodes. The lymphatics draining the middle or thoracic segment pass to the posterior mediastinal glands, while those of the lower or diaphragmatic segment pass to the celiac plexus of the lymph glands. For the most part, the efferent channels of the posterior mediastinal glands pass directly to the thoracic duct, while a few pass to the bronchial glands, which in turn drain into the thoracic duct. Among the afferent channels of the celiac plexus, besides those from the esophagus, are those from the hepatic, gastric, pancreaticosplenic, and lumbar nodes, while the efferents pass to the thoracic duct.

It is well known that carcinomata usually metastasize through the lymphatic system, yet there seem to be very good reasons for the belief that in some instances dissemination of the tumor tissue from the primary focus may be affected through the blood-vascular system, and in some instances it seems possible to take place over mucous or serous surfaces. Let us discuss the several cases seriatim.

Case I showed the carcinoma involving the cervical esophageal segment, but no metastatic growths were noted. Perforation of the trachea, however, had occurred. In Case II, unfortunately, the autopsy record failed to reveal the segment in which the primary tumor was found. There was widespread metastasis as before noted. Case III showed the tumor in the diaphragmatic portion of the tube, but no metastases had developed. Case IV showed the tumor in the lower portion of the tube as a very dense fibrous mass, but no metastases. Tuberculous laryngitis was a complication. Case V showed the growth in the lower segment of the esophagus, with the development of metastases to the pancreas, liver, and lungs. Explanatory of the abdominal and thoracic metastases it seems reasonable to suppose that dissemination occurred through the bloodvessels for two reasons—an absence of involvement of the celiac plexus of nodes and the finding of emboli composed of masses of squamous epithelium in the bloodvessels of the lungs. The probability is that the esophageal veins were effective in distributing the cancerous material with the lungs as the primary seat of deposit. Destruction of pulmonary tissue by the tumor process would facilitate its transmission to the pancreas and liver by way of the arterial system. Case VI

showed the tumor in the upper portion of the esophagus, but no metastases were noted. Case VII showed the tumor in the thoracic segment of the organ, with metastatic deposits in the liver, kidneys, stomach, posterior mediastinal, bronchial, hepatic, and lumbar glands. Involvement of the mediastinal and bronchial glands was naturally direct. The primary tumor mass had extended to the root of the lungs. In the stomach it was only in the muscular coats. It seems most reasonable that in this case dissemination took place through the vascular system, with the root of the lungs as the probable point of entrance of the cancer tissue into the blood. The involvement of the hepatic and lumbar glands was probably secondary to the involvement of the organs drained by these glands.

Case VIII showed the cancer in the diaphragmatic segment of the esophagus, but there were metastases to the posterior mediastinal glands. It is evident that the tumor area was drained by the thoracic lymphatics. In Case IX the location of the cancer was not indicated upon the record. Metastatic deposits were found in the stomach, and are explainable possibly by continuity of structure. Case X showed the tumor in the thoracic portion of the esophagus, and secondary growths were found in the stomach, pancreas, and bronchial glands. The presence of the gastric tumor may be explained as above, while the tumor of the pancreas probably developed by contiguity of structure directly from the stomach. Unquestionably the posterior mediastinal glands were affected to allow extension to the bronchial glands.

The conditions herein brought forth appear sufficient to warrant the statement that the secondary tumors developed not only through the channels of the lymphatic system, but also through the blood-vascular system. It seems possible that metastases may also take place over mucous surfaces.

In the consideration of the present series of carcinomata relative to the frequency of the same, the results show that of 1720 deaths, 8 were associated with the esophageal tumor, or a frequency of 0.46 per cent. These embrace the autopsy records from 1897 to 1907. During this period all records were filed, and the percentage, therefore, is an accurate one. Another point revealed is the preponderance of the squamous-celled tumor over that of the columnar-celled type. But one case of the latter type of tumor was found during the above-mentioned

period. There is a presumption that the tumor of the esophagus with "epithelial pearls" does not metastasize as frequently as does that without "pearls." Probably the same condition is true in this instance that applies to the reason why columnar-celled cancers metastasize with greater facility than do squamous-celled cancers. A resemblance of the cells of the basal cellular type to those of the columnar-celled type of tumor is assumed, so that the spinal cellular type (with "pearls") would appear to be, of all malignant epithelial tumors, the least likely to metastasize. Probably the shape of the cells and a difficulty in adapting themselves to the lumina of the smaller radicles of the lymph and blood-vascular systems render dissemination more difficult. The development of secondary tumors appears not unusual in squamous-celled cancers of the esophagus.

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October 24, 1907.

**Purulent Cerebrospinal Meningitis Caused by the Typhoid Bacillus,  
without the Usual Intestinal Lesions of Typhoid Fever.**

By J. NORMAN HENRY, M.D., AND RANDLE C. ROSENBERGER, M.D.

WILLIAM W., colored, aged thirty-four years, a native of Virginia, a coal picker by occupation, was admitted to the Philadelphia General Hospital, to the service of Dr. F. P. Henry, on account of headache, dizziness, constipation, and fever. His father and mother are dead; causes unknown. His wife and one child are living and well. He had had the ordinary diseases of childhood; otherwise he has always been healthy. The present illness began six days before admission, with headache, dizziness, and vomiting. He went to bed the next day, and was delirious on the third day. Severe pain in back of head, and some pains in legs were his complaints. He had some fever, but no epistaxis. He passed fairly large quantities of urine.

On physical examination he was a large, muscular, well-nourished negro, who lay in bed with his head slightly retracted, very restless, groaning, and picking at the bedclothes. He was profoundly unconscious. The eyes showed marked congestion of bulbar and tarsal conjunctivæ, and slight ptosis of both lids. The eyes were drawn upward and to the left. The pupils were small, equal, but did not react to light. There was some mucopurulent discharge from the conjunctivæ. The tongue was coated, dry, and fissured. Sordes were on the lips and teeth; the breath was foul, but had no characteristic odor. The pulse was rapid, regular, and the tension high. The pulmonary resonance was good throughout. The breath sounds were loud and clear. A few moist rales were heard at the right base. The heart was normal. The abdomen was rigid, but no special areas of tenderness could be palpated. Liver dulness seemed to be normal. Spleen could not be palpated. The arms were flexed and held stiff; the legs were tossed about. The knee-jerks were about normal, the right slightly more prompt than the left. Plantar irritation caused the foot to be drawn up, and the toes to be flexed on both sides. The spine was rigid and slightly concave. The neck was rigid. Kernig's sign was present.

*April 4.* Lumbar puncture was performed and about 25 c.c. of a turbid fluid withdrawn, which, on standing, deposited a heavy purulent sediment.

*April 5.* Kernig's sign was still present; the arms were somewhat rigid. The knee-jerks were absent; plantar irritation elicited no response. Still profoundly unconscious. Lumbar puncture was again performed, 30 c.c. of turbid fluid withdrawn, and 3000 units of diphtheria antitoxin and 30 minims of lysol were injected into the canal. Hot packs seemed to have beneficial effects on convulsions, which were not so frequent or severe.

*April 6.* The condition grew worse. Examination of fluid from the spinal canal showed no diplococci of Weichselbaum, but an organism which looked like the typhoid bacillus. Leukocytes, 14,000; Widal suggestive. Pulse rapid, weak, and almost imperceptible. Urine analysis: Amber; flocculent; acid; 1030; hyaline casts; a few large amorphous urates. Died at 5.15 P.M.

The cerebrospinal fluid was cloudy, alkaline in reaction, and contained small coagula. Cystoscopic examination showed 96 per cent. polynuclear cells, 2 per cent. lymphocytes, and 2 per cent. hyaline cells. Shreds of fibrin were also present. Bacteriological examination showed numerous bacilli, intracellular and extracellular, principally in the polynuclear cells, though a few were also seen in the hyaline forms and lymphocytes. These organisms possessed the morphological and tinctorial properties of a typhoid-like organism.

Inoculations made into various culture media gave rise to a growth of an organism which resembled the typhoid bacillus: that is, grayish-white growth on agar, cloudiness in bouillon, slight acidulation without coagulation in milk, no gas production in lactose or saccharose media, no liquefaction of gelatin, and no indol production in cultures. This organism resembled in all particulars the bacteria observed in spreads, and was agglutinated in dilutions of 1 to 40 with a known typhoid serum and with the serum of the patient.

Five c.c. of blood was obtained (under aseptic precautions) from the vein of the arm and inoculated into 200 c.c. of bouillon. A growth was observed in twenty-four hours, and consisted of an extremely motile bacillus, Gram negative, and resembling in subcultures upon various media the organism obtained from the cerebrospinal fluid.

Agglutination was positive in dilutions of 1 to 40 with the patient's serum and also with a known typhoid serum. Inoculations of 2 c.c. of a forty-eight-hour bouillon culture into the subcutaneous tissue of a guinea-pig failed to produce any pyogenic process.

At autopsy spreads and inoculations were made from the pus upon the brain. The spreads contained an organism identical with that observed in the cerebrospinal fluid during the life of the patient. A Gram negative motile bacillus was obtained which corresponded in all particulars with the organism isolated from the blood during life. Sections of the cord and cerebellum were stained with Loeffler's methylene blue and eosin, polychrome blue and eosin, and by the Gram-Weigert technique. Numerous intracellular and extracellular organisms were found, resembling the bacilli encountered in spreads and cultures; they were especially abundant in the cord.

This organism, from its morphological, tinctorial, and biological character, resembled in all particulars the *Bacillus typhosus*.

Certain of the autopsy notes (made by Dr. A. J. Smith) are of particular interest: The spleen weighs 110 grams, and is not adherent; capsule is smooth and thin; the organ is of a dark-slate color, rather flaccid, and cuts with normal resistance. Cut surface, dark red; Malpighian bodies enlarged; vessels and trabeculae not prominent. The intestines throughout are normal on the exterior; show venous congestion, and walls are quite thin. Mucous membrane of small intestine normal; toward ileocecal valve the membrane is injected, becoming red, and close to valve marked by points of hemorrhage. No follicular enlargement. Peyer's patches are large in their flat extent, but not raised; are pale and show no signs of typhoid medullary swelling or ulceration. Large intestine normal externally and in thickness of wall; likewise shows venous congestion. Mucous surface is moderately congested in upper part; shows no ulceration. Appendix 8 cm. long, of normal caliber, extends toward median line, and is adherent to posterior peritoneal surface. The lumen opened, the mucous surface shows follicles as tiny, black spots; no ulceration. Mesenteric glands are slightly enlarged, fleshy in consistency, reddened in color. Kidneys show nothing indicative of typhoid infection. Dura mater is tense and congested; upon removal the pial vessels are deeply injected and their course marked out by surrounding

yellowish lines of pus; no excess of meningeal fluid. At the base of the brain, about the pons and medulla, extending into the spinal cord, a large amount of pus wells out as in an abscess. Exposure of middle ear fails to show the presence of pus. Dura over base shows no evidence of extension of disease from nasal portion. Cord shows infection of vessels outside of dura throughout its extent, and, especially in upper two-thirds, it is covered with a purulent exudate, similar to that present upon the base and convexity of the brain.

*Pathological Diagnosis.* Purulent cerebrospinal meningitis; cloudy swelling of the liver and the kidneys; acute catarrhal enteritis, with enlargement of Peyer's patches.

The case reported is unusual because of presenting a purulent lesion caused by typhoid bacilli and because of the absence of the customary intestinal lesions of typhoid fever. The patient died on the ninth day of his illness and the autopsy showed that beyond a very little enlargement of the mesenteric glands and a slight change in Peyer's patches, which change might easily be accounted for by the enteritis which was present, the patient showed no typical typhoid lesions.

A bacillus in pure culture, which seems fairly identified as the bacillus of Eberth, was isolated from the blood and spinal fluid, from spreads and inoculations from the pus upon the brain, and was found in sections made from the cord and cerebellum.

Cole<sup>1</sup> reviews the literature of typhoid meningitis. He speaks of 14 cases reported by various authors in which there had been present purulent, fibrinopurulent, or hemorrhagic purulent meningitis, with general typhoid lesions. In 1 case, however, no autopsy was obtained. He also mentions 13 cases of similar purulent meningitis in which, however, the identification of the typhoid bacillus was not so certain, and of several cases in which there was mixed infection with other germs and the typhoid bacillus.

Neumann and Schaeffer report a case similar to ours in that there was present purulent cerebrospinal meningitis without the usual typhoid lesions, and though the organism isolated by them from the

<sup>1</sup> Johns Hopkins Hospital Reports for 1905.

pus appeared in many respects similar to the bacillus of Eberth, yet they did not feel altogether satisfied to place it definitely in that class.

MacCallum reviews at length the pathology of the condition, and finds "nothing peculiar in the histological study of typhoid meningitis unless it be the relative abundance of large phagocytic cells, found particularly about the veins, and also scattered through the tissues."

In our case there were a large number of polynuclear and mononuclear cells, but the large phagocytic cells did not predominate. In this instance the meningitis appears to have been a primary lesion due to the typhoid bacillus, and the intestines to have escaped the ordinary lesions which would be expected to be present at the ninth day of typhoid fever. The history was very carefully reviewed in regard to the possibility of the patient having had typhoid fever at a recent date, and the first statement that the man had been ill but six days before admission was firmly adhered to.

*June 13, 1907.*

### **Sarcoma Arising from the Thymus Gland in an Adult; an Associated Endothoracic Goitre.**

BY JOHN FUNKE, M.D.

THE material forming the basis of this paper is from an autopsy at the Philadelphia Hospital. The body was that of an adult male, aged forty-eight years. There was no evidence of the existing new-growth during the life of the individual, as there were no symptoms referable to such a condition; the clinical diagnosis was myocarditis and chronic interstitial nephritis.

At postmortem the lesions found were as follows: chronic endocarditis, emphysema (bilateral), pyelonephritis, suppurative ureteritis, suppurative cystitis, hypertrophy of the prostate, mediastinal tumor (sarcoma arising from an ectopic goitre).

When the thorax was opened there was present in addition to the pericardium with its contained heart another structure that looked not unlike a duplicate of the heart. This foreign mass lay on and along the pericardium, being loosely attached to it and extending from the upper

border of the third right costal cartilage to the lower border of the fifth; the greater portion of the mass was retrosternal. It measured 7 by 5 by 4 cm.; it was not firm, was reddish pink in color, presented a comparatively smooth external surface, and contained several cysts which were filled with a dark yellow substance; these cysts were not entirely fluctuating. Incision showed that the mass was encapsulated; the cut surfaces were reddish brown, and resembled those of a parenchymatous goitre. The centre of the mass was occupied by a semi-solid substance; the peripheries were more firm, although not indurated. The cysts contained a semisolid gelatinous substance not unlike colloid. They were situated principally at the upper pole of the mass, from which point a fibrous band projected as far as the upper border of the sternum, where it gradually merged with the surrounding tissue; the band was not connected with the thyroid, which organ occupied its normal position and was not altered. The fibrous prolongation led to the belief that the mass was, perhaps, a part of the thyroid gland.

The diagnosis was, of course, not clear, but the growth was termed a mediastinal tumor, probably a sarcoma arising from an ectopic thyroid.

**HISTOLOGY.** The microscopic examination reveals the fact that the tumor is composed of two distinct parts; sections designated group 1 contain principally thyroid tissue; sections in group 2 contain typical sarcomatous tissue but no thyroid structure.

Sections in group 1 are largely composed of nearly normal thyroid tissue; there are acini present, the diameter of which reaches 0.75 cm., and which are either partially or completely filled with colloid substance containing many vacuoles. The stroma in many places contains, in addition to the acini, collections of epithelial cells the character of which is identical with those of the acini. Although these collections of cells are intimately associated with one another, close study shows that each is surrounded by a delicate strand of fibrous tissue, but, unlike the typical acini, they contain no colloid substance. Woelfler holds that such collections of cells form the basis from which tumors develop.

In one part of these sections is a gland-like area distinctly circumscribed by a delicate fibrous-tissue band. The acini-like structures

of which the area is composed are nearly uniform in diameter, and are lined by a single layer of epithelial cells which rests upon a very thin strand of fibrous tissue. In but one section do these acini-like structures contain colloid substance. About the centre of this particular gland-like area are five acini which are separated from the surrounding structure by fibrous tissue and are about to coalesce, the outlines of each being almost obliterated.

Along one margin of sections of group 1 are a few cells like those constituting the greater part of sections of group 2.

The last-named sections contain a band of dense, wavy, fibrous tissue in which there are but few cells, except at a few points where this band contains and surrounds collections of what are undoubtedly lymphoid cells. Usually along one margin, but now and then within the fibrous-tissue band, are masses of other cells constituting the greater part of the sections. Among these cells are bloodvessels and fibrous-tissue trabeculæ, the latter arising from the broad band already mentioned. The elements of the cellular mass are, as a rule, large, round, or oval and closely packed. The protoplasm is not scanty and is not uniform in density; the perinuclear portion of the protoplasm is so rarefied that spaces appear to exist at these points, while the periphery of the protoplasm is more dense, but not granular; with Mallory's reticulum stain it takes a bluish tinge, and under low magnification seems to be an intercellular substance. The nuclei vary in size: some are circular, others are oval; some contain considerable, others little chromatin. For the most part there is no definite arrangement of the cells; at a few points, however, they are placed at right angles to what appear to be bloodvessels in some, and in other instances to bear but little resemblance to such structures. At these points there are at least two, sometimes three or four, strata of cells arranged in this manner. Here the packing of the cells is very much closer; the protoplasm can scarcely be identified.

The structures enclosed by the vertically placed cells have peripheries made up of hyaline fibrous tissue, which encloses cells the nuclei of which stain poorly and are spindle-shaped; the protoplasm is slightly granular. Then, too, there are present fragments of cells, nuclei, and an occasional polymorphonuclear leukocyte. In other places the fibrous sheath encloses not only cells like those just described,

but also erythrocytes. Here the nucleated cells are closely packed and the nuclei are spindle shaped; occasionally these cells tend toward concentric arrangement. Now and then the vertically placed cells enclose structures which are composed of hyaline fibrous tissue only.

In the fibrous tissue principally, but also occasionally among the cellular elements, are cells the nature of which correspond to those first described by Henle in 1865, and later by Stilling, who termed them "chromophile," because of their affinity for the chrome salts.

The bloodvessels are present in considerable numbers; their walls are at times extremely thin, and their lumina are nearly always filled with erythrocytes, leukocytes, and occasionally tumor cells. Besides the vessels with definite walls there are large blood spaces with apparently no walls, allowing many erythrocytes to mingle with the tumor cells.

With regard to the diagnosis, one can say positively that sections in "group 1" are ectopic or accessory thyroid tissue, and in all probability the nodule in these sections is an adenoma. The diagnosis of the tissue in sections, "group 2," is clear, I believe, as to the nature of the tumor, which I hold as a sarcoma, but the source of this growth is somewhat obscure. I admit that the structures enclosed by the vertically placed tumor cells are not all typical corpuscles of Hassel, but some of them do, it appears to me, resemble those structures very closely. Then, too, the lymphoid tissue found in the dense fibrous band simulates thymus-gland tissue.

Dugeon is convinced that, if searched for, the thymus gland would be found in most adults. He states that the corpuscles of Hassel in the adult gland may be hyaline, granular, or calcareous. Virchow maintained that a persistent thymus may become hyperplastic, and later take on a malignant nature in the form of a lymphosarcoma. In a recent communication to the Philadelphia Pathological Society, A. J. Smith produced evidence in support of Afanassieff's view that the corpuscles of Hassel are not vestigial epithelial remnants, but that they develop from vascular endothelium, which, if true, would furnish another source for the development of sarcomata.

In 1849, Gairdner reported a tumor of the mediastinum which he said grew from the thymus gland; Steudener reported a similar growth.

He found what he termed thymus rests, which were composed of small, round lymphoid cells. The growth was the size of an apple, and he maintained it was a hemorrhagic, small, round-celled sarcoma. Sir Astley Cooper, in his work on *The Anatomy of the Thymus Gland*, writes of carcinomata of this organ. Oser, Hedenius, Bramwell, Bienwalt, and also Hahn and Thomas report sarcomata arising from the thymus. Oser's case was a lad aged nineteen years, and Bienwalt's was a woman aged twenty-five years. The authors who mention the fact at all state that the corpuscles of Hassel were not present. Friedleben maintains that these structures are never present after twenty years.

It is not an infrequent occurrence to find thyroid tissue in the superior mediastinum. Richardson holds that just as the middle portion of the thyroid gland may form a pyramidal lobe above the lateral lobe, so in the same manner a pyramidal lobe may grow downward which may later separate from the thyroid and constitute an endothoracic thyroid. Paltauf, in reporting a case of intratracheal goitre, maintained that the ectopic tissue reached the walls of the trachea by direct extension from the normal thyroid or from the parathyroids. Cohnheim, Hollis, and recently Oberfeld and Steinhäus have reported cases of metastasis of thyroid tissue; the metastatic growth mentioned by the last named-authors, after removal, returned a year later, and then the patient died greatly emaciated. They hold that the microscopic pictures of the metastatic growths were identical with the normal gland.

It is, of course, possible that the tumor in the case reported in this paper arose from the ectopic goitre, but then I cannot account for the collections of lymphoid cells and the peculiar bodies surrounded by the tumor cells.



